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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/704,319	11/02/2000	Hiroo Kumagai	1514-00	4918

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EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/704,319	Applicant(s) KUMAGAI ET AL.	
	Examiner Robert Landsman	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *7-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-11* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 November 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Election/Restriction

A. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-6, drawn to a method of examining a disease, comprising measuring the concentration of plural opioid peptides, classified in class 435, subclass 7.1.

II. Claims 7-11 drawn to a method of examining a disease, comprising measuring the concentration of plural opioid receptors, classified in class 435, subclass 7.1.

B. The inventions are distinct, each from each other because of the following reasons:

Inventions I and II are independent and distinct, each from the other, because the methods are practiced with materially different process steps for materially different purposes and each method requires a non-coextensive search because of different starting materials, process steps and goals.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and recognized divergent subject matter as defined by MPEP § 808.02, the Examiner has *prima facie* shown a serious burden of search (see MPEP § 803). Therefore, an initial requirement of restriction for examination purposes as indicated is proper.

C. A telephone call was made to Austin Miller on March 14, 2002 to request an oral election to the above restriction requirement. Applicants elected Group I, claims 1-6, with traverse.

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR § 1.48(b) and by the fee required under 37 CFR § 1.17 (h).

2. Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Method for examining the involvement of opioid peptides in pruritis.

3. Specification

The disclosure is objected to because of the following informalities: there are numerous grammatical errors in the specification. It is recommended that Applicants proofread the specification in order to have the specification read more clearly in english.

4. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for examining pruritis in a patient comprising measuring the concentration of opioid peptides to determine whether opioids are involved in the disease, does not reasonably provide enablement for a method for examining any and all diseases in a patient comprising measuring the concentration of opioid peptides to determine whether opioids are involved in *any and all* of said diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive regarding Applicants claiming a method for examining **any and all diseases** in a patient comprising measuring the concentration of opioid peptides to determine whether opioids are involved in *any and all* of said diseases. Applicants have only demonstrated that opioid receptors, and their peptides, are involved in pruritis and Applicants have only provided guidance and working examples that pruritis may be linked to imbalances of various opioid peptides, or opioid receptors, in the body. Furthermore, Applicants have only demonstrated that mu and kappa opioid receptors are linked to pruritis, and no tests have been performed, or data shown, which relates the role of delta opioid receptor expression to this disease.

However, Applicants are claiming that they can determine whether opioid peptides are involved in *any and all* diseases. Applicants provide no guidance or working examples for determining whether

opioid peptides, are involved in diseases other than pruritis. It is possible that opioid peptides can be upregulated or downregulated in a patient for reasons not linked to the disease being studied. For example, a patient may have a genetic cause of altered peptide levels. Similarly, the patient may have altered levels of opioid peptides due to a condition unrelated to the disease being studied. Applicants have not taught the artisan how to conclude that opioid receptors are involved in a particular disease other than pruritis. Therefore, it is not predictable to the artisan how to determine whether opioids are involved with the disease being studied.

Similarly, Applicants have only provided guidance and working examples that 3 opioid peptides, β-endorphin, Leu-enkephalin and dynorphin A, and not the **excessive breadth of claimed opioid peptides** which were obtained **only from peripheral blood** and not from all blood cells, body fluids, or tissues were indicative of itching. Again, the breadth of the claims is excessive with regard to Applicants claiming the ability to determine whether opioids are involved in a disease by measuring any and all opioid peptides in any blood cell, body fluids, or tissue. Applicants have not enabled the ability to determine if opioids were involved in a disease by measuring, for example, the ratio of opioid peptides in brain tissue, lymph, aqueous humor in the eye, etc, but have only correlated opioids with a disease by measuring very specific peptides in very specific fluids (i.e. peripheral blood).

In summary, due to the excessive breadth of the claims for determining whether opioid peptides are involved in diseases other than pruritis, for claiming the ability to determine whether opioids are involved in a disease by measuring any and all opioid peptides in any blood cell, body fluids, or tissue as well as the lack of guidance and working examples of diseases which present with an opioid imbalance other than pruritis and the inability to conclude that opioid peptides, are involved in the disease being studied, along with the unpredictability to the artisan how to determine that altered opioid peptide levels are, in fact, involved in said disease, the Examiner holds that undue experimentation is necessary to practice the invention as claimed.

5. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "plural" is confusing. It is suggested that this term be replaced with, for example, "numerous types," or "various types." Claims 3-6 are rejected since they depend from rejected base claims.

6. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Simonnet et al. (Neuropeptides 7(3):229-40, 1986). The claims recite a method for examining a disease by measuring the concentrations of opioid peptides in a bodily sample and calculating the ratio of said concentrations to determine whether opioids are involved in the disease. Simonnet et al. teach measuring the levels of radio-immunoassayable methionine-enkephalin (ME) and radioreceptor-active opiate peptide levels (OP) in CSF from patients with and without chronic pain. The authors made various conclusions to the disease of chronic pain based on the ME/OP ratio (Abstract).

B. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Ripamonti et al. (Ann Oncol 1998 Jan;9(1):79-83). The claim recites a method for examining a disease by measuring the concentrations of opioid peptides in a bodily sample and calculating the ratio of said concentrations to determine whether opioids are involved in the disease. Ripamonti et al. teach measuring the levels of hydromorphone and methadone in subjects with cancer pain. Ripamonti et al. meet the limitations of the claims since the claims do not recite that the opioid peptides have to be endogenous. The fact that opioids help alleviate cancer pain demonstrate that opioid peptides are involved in this disease.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
April 08, 2002

GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
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